

Remarks

Reconsideration of this Application is respectfully requested.

Claims 1-3, 6-17, 20-24, 27-37, 73-77, 79-82, 106-109, 112, 140 and 143-174 are pending in the application, with claims 1, 15, 22, 106, 157, 158 and 161 being the independent claims.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider the outstanding rejections and that they be withdrawn.

Claim Rejections Under 35 U.S.C. § 103

Claims 1-3, 6-17, 20-24, 27-37, 73-77, 140, 154 and 157-174 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 4,786,599 to Chessebeuf *et al.* ("Chessebeuf"), in view of U.S. Patent No. 5,728,580 to Shuler *et al.* ("Shuler") and U.S. Patent No. 5,712,163 to Parenteau *et al.* ("Parenteau"). Applicants respectfully traverse this rejection for the reasons set forth in the Reply Under 37 C.F.R. § 1.111, filed on November 26, 2002.

This rejection was earlier set out by the Examiner. (*See* Paper No. 28, page 4.) However, the Examiner asserted that Applicants' November 6, 2002 reply was not persuasive. (*See* Paper No. 32, page 2.) The Examiner apparently alleged that Shuler's teaching of animal cells encompassed insect cells and mammalian cells. However, the Examiner has made no showing to contradict Shuler's teaching that polysulfated polyanions

cause aggregation, *i.e.*, are incompatible with cultivating the cells in suspension culture as featured in the present claims. (See Applicants' Reply Under 37 C.F.R. § 1.111, filed on November 26, 2002, at pages 6-7 and 10-11.)

The Examiner asserted that "[a]ll that is needed in order to establish a *prima facie* case of obviousness is some suggestion to combine the teachings." (Paper No. 32, page 3.) Applicants respectfully submit that this is not the correct legal standard for establishing a *prima facie* case of obviousness. The proper standard, as instructed in the MPEP, is found in the following paragraph:

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. "*The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art.*" *In re Kotzab*, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). See also *In re Lee*, 277 F.3d 1338, 1342-44, 61 USPQ2d 1430, 1433-34 (Fed. Cir. 2002) (discussing the importance of relying on objective evidence and making specific factual findings with respect to the motivation to combine references); *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

(MPEP § 2143, emphasis added.) Applicants respectfully submit that, according to the correct legal standard and the guidance provided by the MPEP, combined teachings, knowledge, and nature of the problem must be considered as a whole. Thus, proper application of combined teachings requires that Shuler be considered for all it teaches. The teachings relating to aggregation of mammalian cells must be considered as teaching away

from combining the references, as proposed by the Examiner, to arrive at the presently claimed invention.

See also MPEP § 2145.X.D:

***D. References Teach Away from the Invention or
Render Prior Art Unsatisfactory for Intended
Purpose***

In addition to the material below, see MPEP § 2141.02 (prior art must be considered in its entirety, including disclosures that teach away from the claims) and MPEP § 2143.01 (proposed modification cannot render the prior art unsatisfactory for its intended purpose or change the principle of operation of a reference). (Emphasis added.)

Thus the MPEP, when read in context, clearly requires further consideration by the Examiner of all the teachings in their entireties. When the references cited by the Examiner are considered in their entireties, it must be concluded that the references do not establish a *prima facie* case of obviousness. Reconsideration and withdrawal of this rejection are respectfully requested.

With specific reference to HEK 293 cells, the Examiner stated, "such cells would not have been expected to be cultured any differently from other animal cell lines disclosed in the art and based on knowledge generally available to one of ordinary skill in the art." (Paper No. 32, page 3.) The Examiner has not presented any evidence to support this position. Thus, it appears that the Examiner has taken "official notice" of what would (or would not) have been expected in the art with respect to HEK 293 cells. Applicants respectfully submit that the Examiner's assertion regarding HEK 293 cells is incorrect and, moreover, the Examiner has not followed instructed procedure for taking official notice. According to the MPEP:

**2144.03 Reliance on Common Knowledge in the Art or
"Well Known" Prior Art [R-1]**

****>**In limited circumstances, it is appropriate for an examiner to take official notice of facts not in the record or to rely on "common knowledge" in making a rejection, however such rejections should be judiciously applied.

**PROCEDURE FOR RELYING ON COMMON
KNOWLEDGE OR TAKING OFFICIAL NOTICE**

The standard of review applied to findings of fact is the "substantial evidence" standard under the Administrative Procedure Act (APA). See *In re Gartside*, 203 F.3d 1305, 1315, 53 USPQ2d 1769, 1775 (Fed. Cir. 2000). See also MPEP § 1216.01. In light of recent Federal Circuit decisions as discussed below and the substantial evidence standard of review now applied to USPTO Board decisions, the following guidance is provided in order to assist the examiners in determining when it is appropriate to take official notice of facts without supporting documentary evidence or to rely on common knowledge in the art in making a rejection, and if such official notice is taken, what evidence is necessary to support the examiner's conclusion of common knowledge in the art.

***A. Determine When It Is Appropriate To Take Official
Notice Without Documentary Evidence To Support The
Examiner's Conclusion***

Official notice without documentary evidence to support an examiner's conclusion is permissible only in some circumstances. While "official notice" may be relied on, these circumstances should be rare when an application is under final rejection or action under 37 CFR 1.113. Official notice unsupported by documentary evidence should only be taken by the examiner where the facts asserted to be well-known, or to be common knowledge in the art are capable of instant and unquestionable demonstration as being well-known. As noted by the court in *In re Ahlert*, 424 F.2d 1088, 1091, 165 USPQ 418, 420 (CCPA 1970), the notice of facts beyond the

record which may be taken by the examiner must be "capable of such instant and unquestionable demonstration as to defy dispute" (citing *In re Knapp Monarch Co.*, 296 F.2d 230, 132 USPQ 6 (CCPA 1961)). In *Ahlert*, the court held that the Board properly took judicial notice that "it is old to adjust intensity of a flame in accordance with the heat requirement." See also *In re Fox*, 471 F.2d 1405, 1407, 176 USPQ 340, 341 (CCPA 1973) (the court took "judicial notice of the fact that tape recorders commonly erase tape automatically when new 'audio information' is recorded on a tape which already has a recording on it"). In appropriate circumstances, it might not be unreasonable to take official notice of the fact that it is desirable to make something faster, cheaper, better, or stronger without the specific support of documentary evidence. Furthermore, it might not be unreasonable for the examiner in a first Office action to take official notice of facts by asserting that certain limitations in a dependent claim are old and well known expedients in the art without the support of documentary evidence provided the facts so noticed are of notorious character and serve only to "fill in the gaps" which might exist in the evidentiary showing made by the examiner to support a particular ground of rejection. *In re Zurko*, 258 F.3d 1379, 1385, 59 USPQ2d 1693, 1697 (Fed. Cir. 2001); *Ahlert*, 424 F.2d at 1092, 165 USPQ at 421.

It would not be appropriate for the examiner to take official notice of facts without citing a prior art reference where the facts asserted to be well known are not capable of instant and unquestionable demonstration as being well-known. For example, assertions of technical facts in the areas of esoteric technology or specific knowledge of the prior art must always be supported by citation to some reference work recognized as standard in the pertinent art. *In re Ahlert*, 424 F.2d at 1091, 165 USPQ at 420-21. See also *In re Grose*, 592 F.2d 1161, 1167-68, 201 USPQ 57, 63 (CCPA 1979) ("[W]hen the PTO seeks to rely upon a chemical theory, in establishing a prima facie case of obviousness, it must provide evidentiary support for the existence and meaning of that theory."); *In re Eynde*, 480 F.2d 1364, 1370, 178 USPQ 470, 474 (CCPA 1973) ("[W]e reject the notion that judicial or administrative notice may be taken of the state of the art. The facts constituting the state of the art are normally subject to the possibility of rational disagreement among reasonable men and are not amenable to the taking of such notice.").

It is never appropriate to rely solely on "common knowledge" in the art without evidentiary support in the

record, as the principal evidence upon which a rejection was based. *Zurko*, 258 F.3d at 1385, 59 USPQ2d at 1697 ("[T]he Board cannot simply reach conclusions based on its own understanding or experience-or on its assessment of what would be basic knowledge or common sense. Rather, the Board must point to some concrete evidence in the record in support of these findings."). While the court explained that, "as an administrative tribunal the Board clearly has expertise in the subject matter over which it exercises jurisdiction," it made clear that such "expertise may provide sufficient support for conclusions [only] as to peripheral issues." *Id.* at 1385-86, 59 USPQ2d at 1697. As the court held in *Zurko*, an assessment of basic knowledge and common sense that is not based on any evidence in the record lacks substantial evidence support. *Id.* at 1385, 59 USPQ2d at 1697. See also *In re Lee*, 277 F.3d 1338, 1344-45, 61 USPQ2d 1430, 1434-35 (Fed. Cir. 2002) (In reversing the Board's decision, the court stated " 'common knowledge and common sense' on which the Board relied in rejecting Lee's application are not the specialized knowledge and expertise contemplated by the Administrative Procedure Act. Conclusory statements such as those here provided do not fulfill the agency's obligation. The board cannot rely on conclusory statements when dealing with particular combinations of prior art and specific claims, but must set forth the rationale on which it relies.").

(MPEP § 2144.03, emphasis added.) In view of the above, Applicants respectfully submit that this rejection is not proper and that withdrawal of the rejection is appropriate.

With respect to proteins in cell culture medium, the Examiner stated that "protein is a well known contaminant of cell culture medium." (*See* Paper No. 32, page 3.) Applicants respectfully point out that cell culture medium is synthesized. Thus the proteins present are not contaminants, but are intentionally added ingredients. Proteins such as insulin and transferrin and protein-containing mixtures such as serum have been conventionally added to culture. While it may be desirable to use a protein-free medium, substitutes for the conventionally added proteins are preferably added to obtain acceptable culture conditions. The Examiner's allegations based on the incorrect assumption that proteins are contaminants

cannot be properly relied upon in maintaining the rejection. In view of this, Applicants respectfully submit that this rejection is improper and that withdrawal of the rejection is appropriate.

Similarly, the Examiner has apparently taken official notice that protein would serve no function in cell culture medium. According to the Examiner, "the protein would serve no function to a method for culturing the cells in the cell culture medium from which the protein has been eliminated due to its undesirable effect and function." (Paper No. 32, page 3.) This noticed fact is incorrect and the notice thereof was improper. For example, please note the conventional addition of protein containing serum to media. Thus, it is clear that proteins have beneficial qualities. However, there is a desire to eliminate undefined components such as serum from media and also to eliminate animal derived components to provide consistency and to remove potential for pathogenic particles. Thus it is incumbent on media developers to find substitutes that provide the desired qualities of proteins without raising the undesirable issues inherent in protein's use. For this additional reason, Applicants respectfully submit that the rejection is improperly maintained. Reconsideration and withdrawal of the rejection are respectfully requested.

Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the

present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Frank R. Cottingham
Attorney for Applicants
Registration No. 50,437

Date: AUG. 25, 2003

1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600